Near-Infrared Spectroscopy for Non-destructive Coating Analysis Calibrated by Terahertz Pulsed Imaging

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***Abstract*— Near-infrared (NIR) spectroscopy is a versatile technique for non-destructive analysis of pharmaceutical tablet coating thickness; however, it needs a calibration model and thus the prior knowledge about the coating thickness of each tablet is required. In this work, we demonstrate that Terahertz Pulsed Imaging (TPI) can provide, in a nondestructive fashion, such coating thickness information for building the calibration model needed by the NIR technique.**

I. Introduction

Coating of pharmaceutical tablets with a polymer film is a common approach to control the release of drug molecules from the dosage form, such as a tablet, in the human body [1]. A coating offers advantages both to consumer and in the pharmaceutical manufacturing process. Therefore non-destructive techniques for characterizing pharmaceutical tablet coatings become increasingly important. Near-infrared (NIR) spectroscopy is a powerful non-destructive tool for the analysis of pharmaceutical tablet coatings [2-7]. Generally, using NIR it is not possible to directly measure the tablet coating thickness. It is possible to determine this property indirectly by applying a calibration model using datasets of samples with known thickness. Typically the weight gain of the tablet during coating is used to build the calibration model [2]. However, it was shown that the coating thickness varies considerably for tablets with the same weight gain (or coating time) [4]. Terahertz Pulsed Imaging (TPI), on the other hand, can provide non-destructively the precise coating thickness of each tablet [8]. In this work, the coating thickness determined using TPI was used to build a calibration model which is subsequently employed to predict the coating thickness of other tablets. We demonstrate that the coating thickness predicted by neural network-based calibration model, are in good agreement with the one measured directly by TPI method.

II. Methods And Results

In total, 68 pharmaceutical tablets with various coating thickness have been investigated using a TPI imaga 2000 (Teraview Ltd, UK) and a NIR256-2.5 spectrometer (Ocean Optics, USA). Terahertz radiation is generated by pumping a biased photoconductive antenna with a laser pulse from a Ti:Sapphire femtosecond laser with a centre wavelength of 800 nm. The emitted terahertz pulse is collected, collimated, and then focused onto a coated tablet. The reflected and backscattered terahertz pulse is then collected and focused onto an unbiased photoconductive antenna for the laser-gated terahertz detection. The NIR fibre optic spectrometer connects to notebook via a USB port and it requires an external +5VDC power supply to power the spectrometer's high-performance InGaAs array detector. The reflectance NIR spectroscopies of the tablets were measured. Fig.1 (a) is the 2D TPI coating thickness map showing the tablet-to-tablet thickness variation for the tablets. This tablet-to-tablet variation is a true representation of the coating thickness, rather than the measurement error as the application of polymer in the coating process is not uniformly distributed over all tablet cores in the coating pan [5]. Fig.1 (b) shows the averaged NIR spectra for the tablets. The arrow indicates the direction of intensity change with increasing coating thickness.

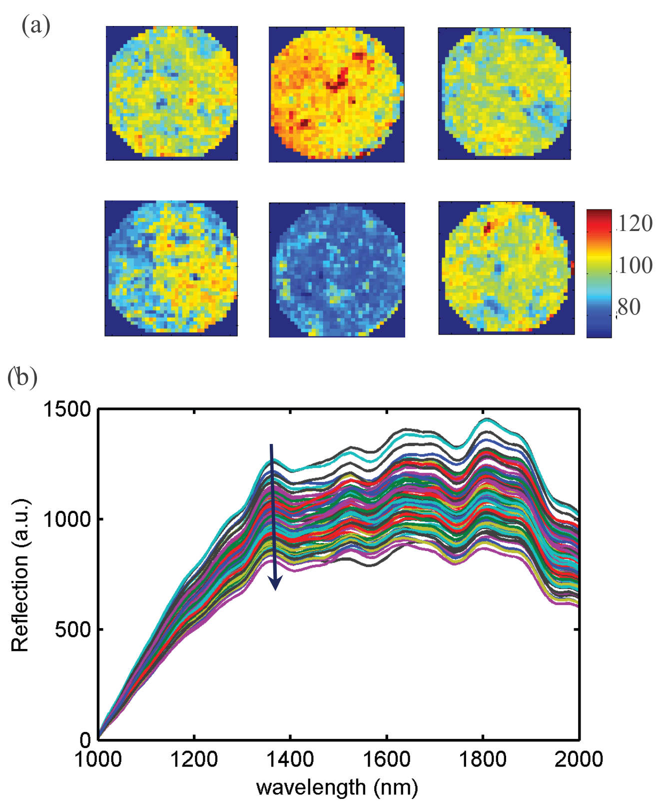

Fig.1 (a) the 2D TPI tablet thickness maps showing tablet-to-tablet thickness variation for the tablets. The size of the maps is 10 mm; (b) Averaged NIR spectra for 68 pharmaceutical tablets. The arrow indicates the direction of intensity change with increasing tablet coating thickness.

The coating thickness calibration model is build by using a neural network method. Neural networks are composed of simple elements operating in parallel. These elements are inspired by biological nervous systems [9]. Typically, neural networks are adjusted, or trained, so that a particular input leads to a specific target output. For our cases, the input parameter is the NIR spectrum and the output one is the known thickness measured by TPI method, as shown in Fig.2. Therefore, the network is adjusted or trained, based on a comparison of the output and the target, until the network output matches the target. Typically, many such input/target pairs are needed to train a network. The neural network computing technique has recently been developed to become one of the very powerful modeling tools. This technique is based on a non-linear statistical approach and is particularly suitable for the nonlinear and complex correlations [10].

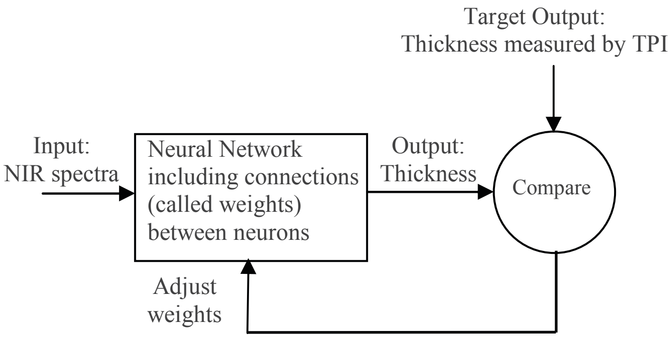

Fig.2 Neural networks training for getting a specific target output by a particular input

In the present work, the NIR spectra measured from upper face of all the tablets are used as the learning data sets. The NIR spectra for the lower face of the tablets are used for the prediction of the tablet thickness. Once the neural network is trained and it can be used to predict the coating thickness using the NIR spectra input.

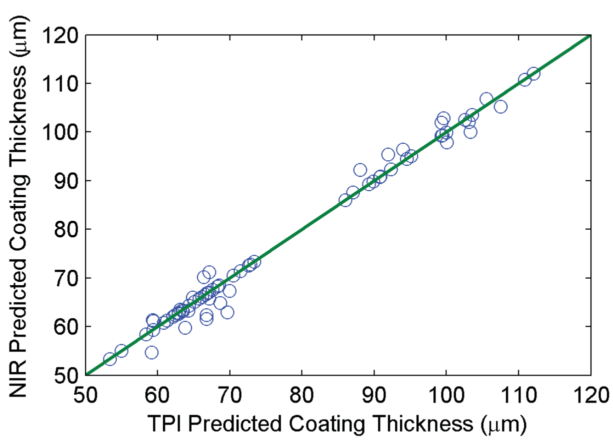

Fig.3 Correlation between TPI predicted coating thickness and NIR predicted coating thickness;

As shown in Fig.3, the coating thickness predicted by the neural network-based calibration model, is in good agreement with the one measured directly by the TPI method. In a conclusion, the results show that in addition to its application as a direct tablet coating thickness imaging instrument [8] TPI can also be used to provide reliable tablet coating thickness values in a nondestructive fashion for building a NIR calibration model. It is noted that in real applications, the reliability of the neural network-based calibration model is reliable on the reliability of the learning data set. More accurate learning data set (TPI and NIR spectra), more robust and reliable neural network-based NIR calibration model.

ACKNOWLEDGEMENT

The authors would like to acknowledge financial support from UK Technology Strategy Board (AB293H).

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